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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,442	07/10/2001	Lawrence M. Kauvar	25352-0003P8-1	8907

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT PAPER NUMBER

1615

DATE MAILED: 03/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,442	KAUVAR ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-60 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-60 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1-23-02</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims included in the prosecution are 1-60.

Claim Rejections - 35 USC § 112

1. Claims 42 and 60 provide for the use of the compounds of the depicted formula, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 42 and 60 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-4, 7-15, 18-24, 27-35, and 38-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Kauvar et al (5,955,432) or WO 96/40205 of record.

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Both Kauvar et al (5,955,432) and WO disclose a method of stimulating hematopoiesis using the same claimed compounds (note the abstract, col. 2, line 30 through col. 8, line 35, examples and claims of US 432; abstract, pages 7-10, Examples and claims).

4. Claims 21-24, 27-35 and 38-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Morgan et al (Cancer Chemother. Pharmacol. 37, 363-370, 1996) of record.

Morgan et al disclose a method of administration of the claimed compounds to potentiate the effect of chemotherapeutic compounds (abstract, Materials and Methods, Tables and Figures).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 5-6, 16-17, 25-26, 36-37 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauvar et al or WO 96/40205 cited above.

As discussed above, Kauvar et al and WO both disclose a method of stimulating hematopoiesis using the same claimed. Although Kauvar et al and WO do not show

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the administration of the compounds in liposomal form, through examples, both suggest the use of liposomes for the delivery of the compounds (see col. 7, lines 17-19 of 432; page 12, lines 27-29 of WO). It would have been obvious to one of ordinary skill in the art to use of liposomes for the delivery of the claimed compounds with a reasonable expectation of success, since liposomes are well known in the art for their advantages and since the reference itself is suggestive of the use of the liposomes.

7. Claims 5-6, 16-17, 25-26, 36-37 and 43-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauvar et al or WO 96/40205 cited above, further in view of the references of Young (5,023,087), Barenholz (5,043,166), Straubinger (5,415,869) or Lambiez (5,605,703) by themselves or in combination.

The teachings of Kauvar et al, and WO have been discussed above. Both are suggestive of the use of liposomes for the delivery of the claimed compounds. What are lacking in these references however, are the teachings of the use of specific liposomes, that is, negatively charged liposomes.

Young while disclosing liposomal formulations for the delivery of a variety of drugs teaches that the liposomes allow the selected compound to be released in the blood stream at a slow, controlled rate over a several hours to several days period, thus avoiding the large fluctuations in drug blood levels that are characteristic of free drug administration. Young further teaches that one advantage of his formulation is the increased stability of a pharmaceutical compound, which is achieved with liposome encapsulation. Young's liposomes are made from egg PC and PG (abstract; col. 7, line

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58 through col. 8, line 18; col. 9, line 65 through col. 10, line 49; col. 16, line 34 et seq., col. 18, line 45 et seq., Examples).

Barenholz teaches that the negatively charged phospholipids such as PG, PS tend to enhance the drug liposome stability (col. 6, line 57 et seq., Tables 3 and 4 and Example).

Straubinger while disclosing liposomal Taxol formulations teaches that liposomes containing PG and PC were physically stable and retained approximately 100% of their Taxol content for more than 2 months (Example 2 on col. 12).

Lambiez while disclosing doxorubicin-containing liposomes teaches that the inclusion of a negatively charged phospholipid favors the stability of the liposome solution.

Lambiez also teaches high encapsulation efficiencies of these liposomes (abstract, col. 4, line 24 et seq., Table II on col.9 and claims).

The use of liposomes, negatively charged liposomes for the delivery of the compounds of Kauvar et al or WO would have been obvious to one of ordinary skill in the art because of the advantages taught by the references of Young, Barenholz, Straubinger, and Lambiez.

8. Claims 25-26, 36-37, 43-52 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al cited above, further in view of the references of Young (5,023,087), Barenholz (5,043,166), Straubinger (5,415,869) or Lambiez (5,605,703) by themselves or in combination.

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The teachings of Morgan et al have been discussed above. What are lacking in Morgan et al are the teachings of the use of liposomes for the delivery of the compounds.

Young while disclosing liposomal formulations for the delivery of a variety of drugs teaches that the liposomes allow the selected compound to be released in the blood stream at a slow, controlled rate over a several hours to several days period, thus avoiding the large fluctuations in drug blood levels that are characteristic of free drug administration. Young further teaches that one advantage of his formulation is the increased stability of a pharmaceutical compound, which is achieved with liposome encapsulation. Young's liposomes are made from egg PC and PG (abstract; col. 7, line 58 through col. 8, line 18; col. 9, line 65 through col. 10, line 49; col. 16, line 34 et seq., col. 18, line 45 et seq., Examples).

Barenholz teaches that the negatively charged phospholipids such as PG, PS tend to enhance the drug liposome stability (col. 6, line 57 et seq., Tables 3 and 4 and Example).

Straubinger while disclosing liposomal Taxol formulations teaches that liposomes containing PG and PC were physically stable and retained approximately 100% of their Taxol content for more than 2 months (Example 2 on col. 12).

Lambiez while disclosing doxorubicin-containing liposomes teaches that the inclusion of a negatively charged phospholipid favors the stability of the liposome solution.

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Lambiez also teaches high encapsulation efficiencies of these liposomes (abstract, col. 4, line 24 et seq., Table II on col.9 and claims).

The use of liposomes, negatively charged liposomes for the delivery of the compounds of Morgan et al would have been obvious to one of ordinary skill in the art because of the advantages taught by the references of Young, Barenholz, Straubinger, and Lambiez.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-38 of U.S. Patent No.

5,955,432. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in both said patent and instant application are drawn to the same compounds and method of stimulating hematopoiesis or method of potentiating a chemotherapeutic compound effect and the claims in the said patent recite esters of the compounds and instant diesters therefore, come under the generic

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term in said patent. Although the claims in said patent do not recite lipid formulations, in view of the language 'comprising' in the claims and reciting of pharmaceutically acceptable excipients, these claims are included in the rejection.

11. Claims 5-6, 16-17, 25-26, 36-37 and 43-60 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-38 of U.S. Patent No. 5,955,432 in view of Young (5,023,087), Barenholz (5,043,166), Straubinger (5,415,869) or Lambiez (5,605,703) by themselves or in combination.

As pointed out above, the claims in said patent do not recite lipid carrier or specifically negatively charged liposomes as carriers. The patent in the specification

however, recites liposomes as carriers.

Young while disclosing liposomal formulations for the delivery of a variety of drugs teaches that the liposomes allow the selected compound to be released in the

blood stream at a slow, controlled rate over a several hours to several days period, thus avoiding the large fluctuations in drug blood levels that are characteristic of free drug administration. Young further teaches that one advantage of his formulation is the increased stability of a pharmaceutical compound, which is achieved with liposome encapsulation. Young's liposomes are made from egg PC and PG (abstract; col. 7, line 58 through col. 8, line 18; col. 9, line 65 through col. 10, line 49; col. 16, line 34 et seq., col. 18, line 45 et seq., Examples).

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Barenholz teaches that the negatively charged phospholipids such as PG, PS tend to enhance the drug liposome stability (col. 6, line 57 et seq., Tables 3 and 4 and Example).

Straubinger while disclosing liposomal Taxol formulations teaches that liposomes containing PG and PC were physically stable and retained approximately 100% of their Taxol content for more than 2 months (Example 2 on col. 12).

Lambiez while disclosing doxorubicin-containing liposomes teaches that the inclusion of a negatively charged phospholipid favors the stability of the liposome solution.

Lambiez also teaches high encapsulation efficiencies of these liposomes (abstract, col. 4, line 24 et seq., Table II on col.9 and claims).

The use of liposomes, negatively charged liposomes for the delivery of the compounds in US 5,955,432 would have been obvious to one of ordinary skill in the art because of the advantages taught by the references of Young, Barenholz, Straubinger, and Lambiez.


12. Claims 29-35 and 38-41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,679,643. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in both said patent and instant application are drawn to the same compounds. Instant claims recite 'pharmaceutical compositions' and there is no patentable distinction between compound claims and composition claims.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.


Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK